Computational Prediction of Microbial Metabolism of Chemical Compounds

with a focus on gut and environmental microbiomes

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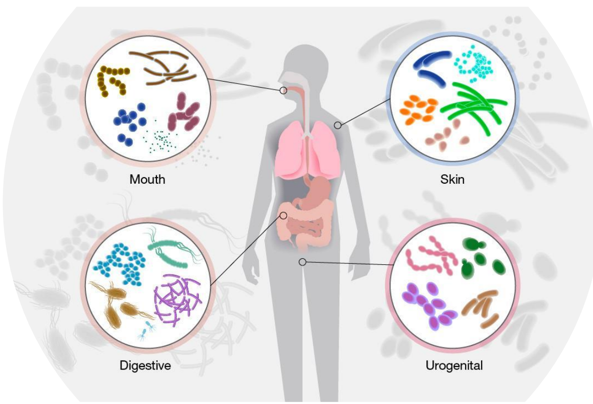
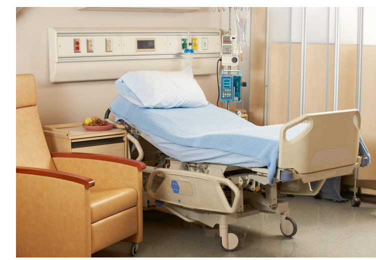
Nexilico develops computational microbiome technologies adaptable to diverse fields and applications

Human health



Environment

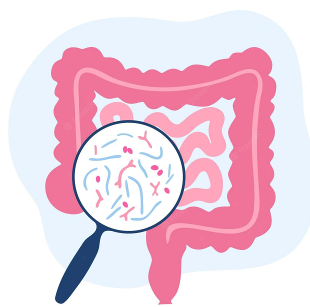
Built Settings



The primary goal is to shed light on the dynamic interactions between microbiomes and their surrounding environments and external stimuli

Predicting microbial metabolism of chemical compounds unlocks applications in gut health and environmental microbiomes

Precision Medicine



Bioremediation

Microvi

Problem Statement

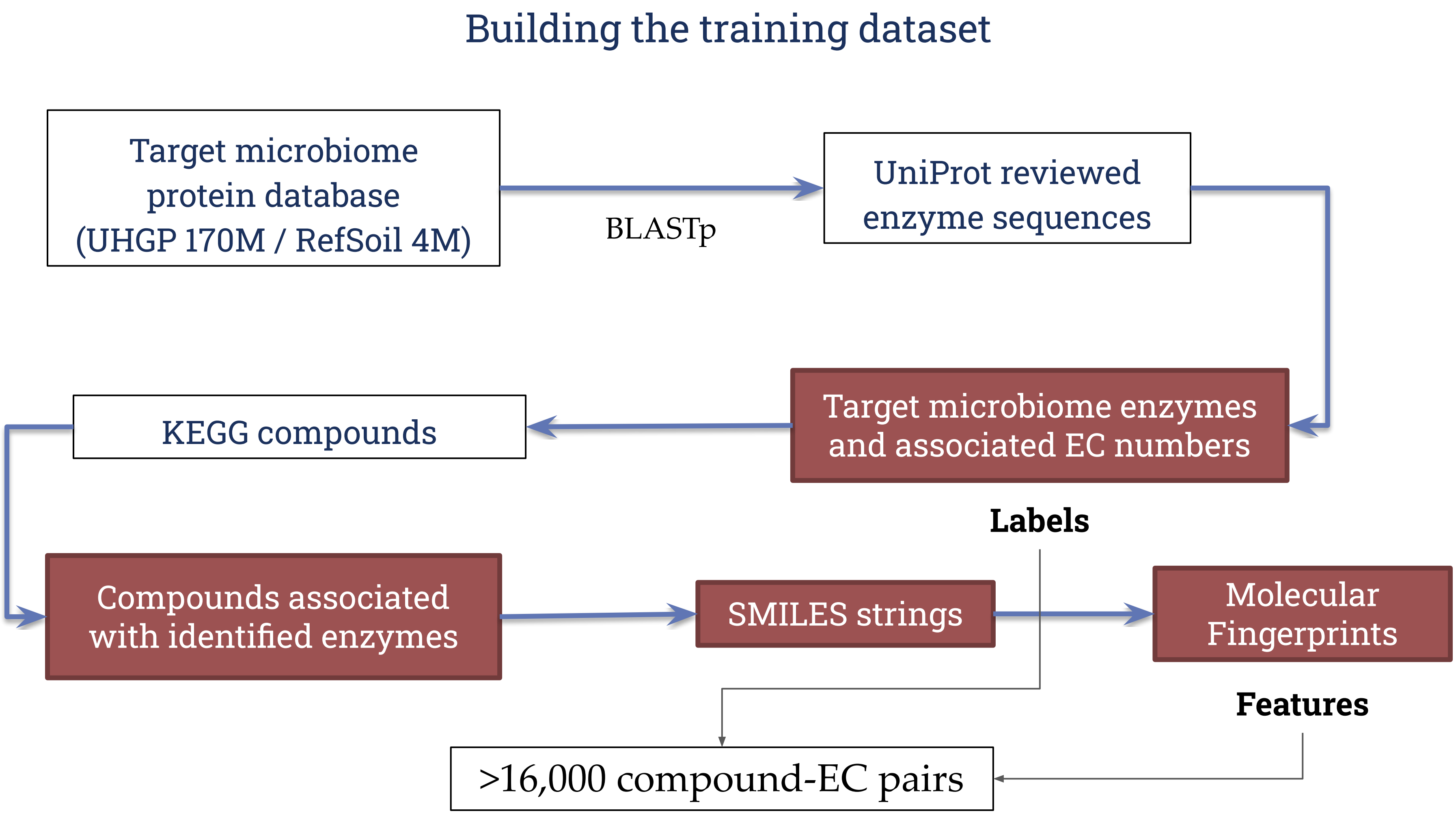
Given a chemical compound structure, predict:

- metabolizing enzymes and microorganisms, and
- time-resolved degradation profile

Compound structural similarity can serve as a proxy for enzyme sharing

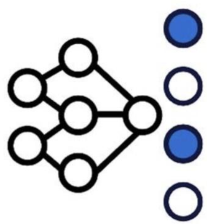
compounds	enzymes
ATP	EC 1.1.1.1
Pyruvate	EC 2.7.1.1
Cholesterol	EC 3.4.21.4
Glutamate	EC 4.2.1.1
Folic Acid	EC 5.3.1.9
Penicillin G	EC 6.3.2.1
Estradiol	EC 1.14.13.39
Ubiquinone	EC 2.3.1.12
Sucrose	EC 3.1.3.1

Target compound



Building the training dataset
Target microbiome protein database (UHGP 170M / RefSoil 4M)
BLASTp
UniProt reviewed enzyme sequences
Target microbiome enzymes and associated EC numbers
KEGG compounds
Compounds associated with identified enzymes
SMILES strings
Molecular Fingerprints
Labels
Features
>16,000 compound-EC pairs

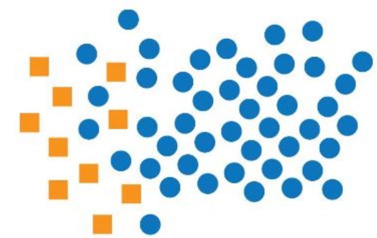
Challenges in the training data



Multilabel

EC: 3.2.1.21

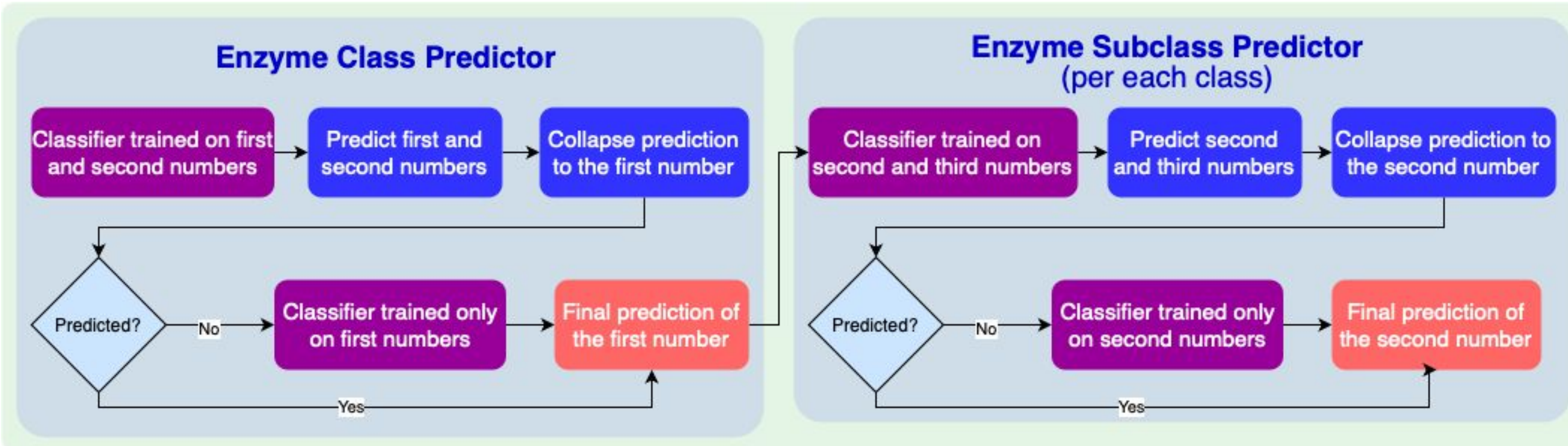
Hierarchical structure



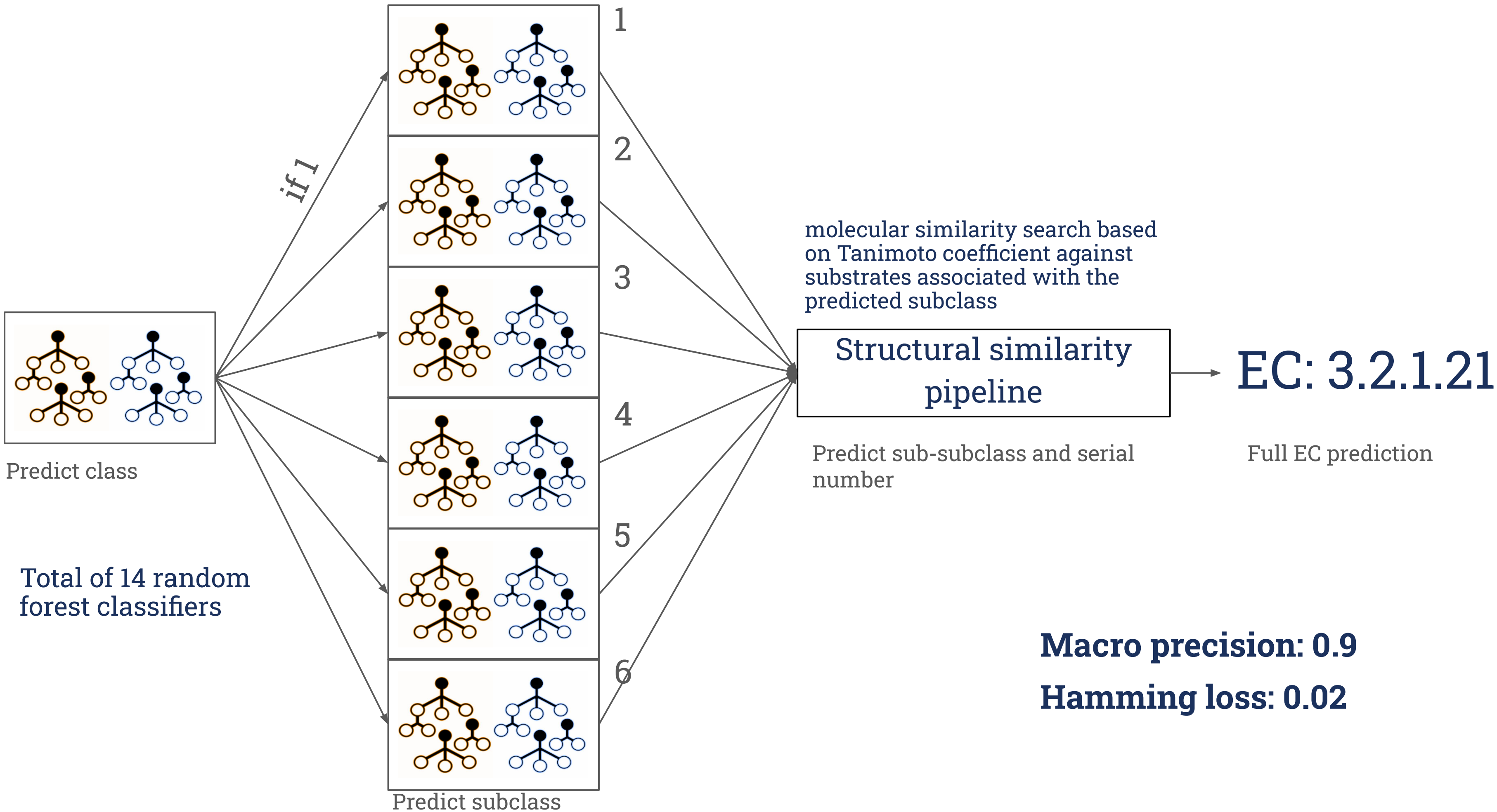
Data imbalance

Typical machine learning classifiers and deep learning models failed to achieve high accuracy.

Introducing multilabel inverse hierarchical (MIH) model



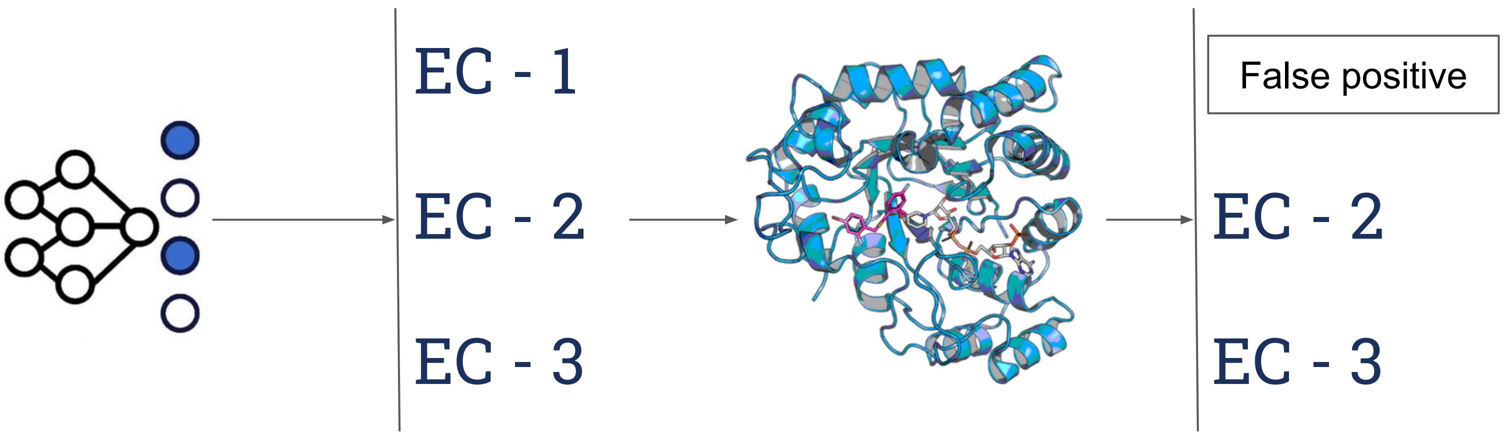
Integrating specificity of ML and sensitivity of structural similarity



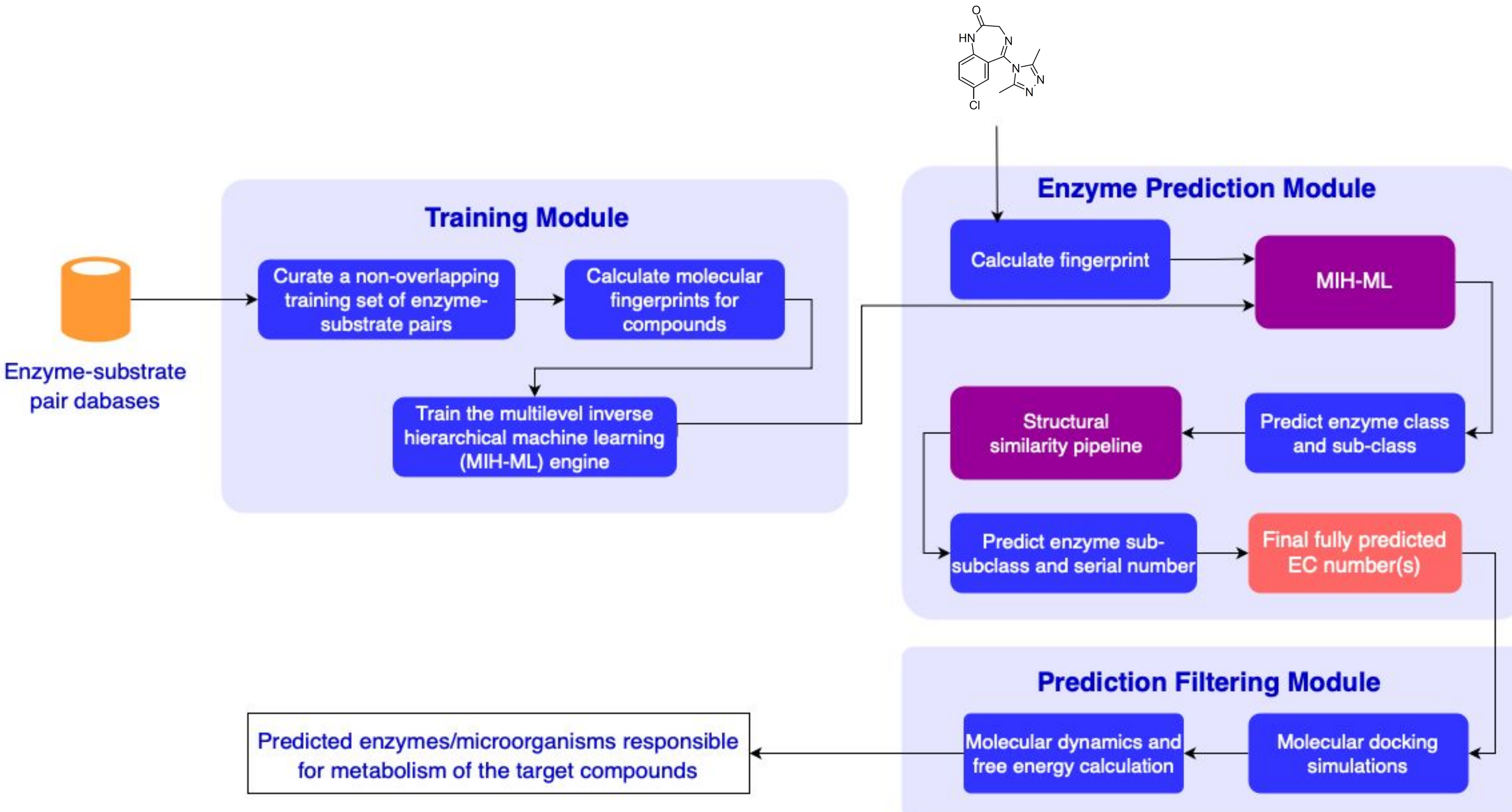
Macro precision: 0.9

Hamming loss: 0.02

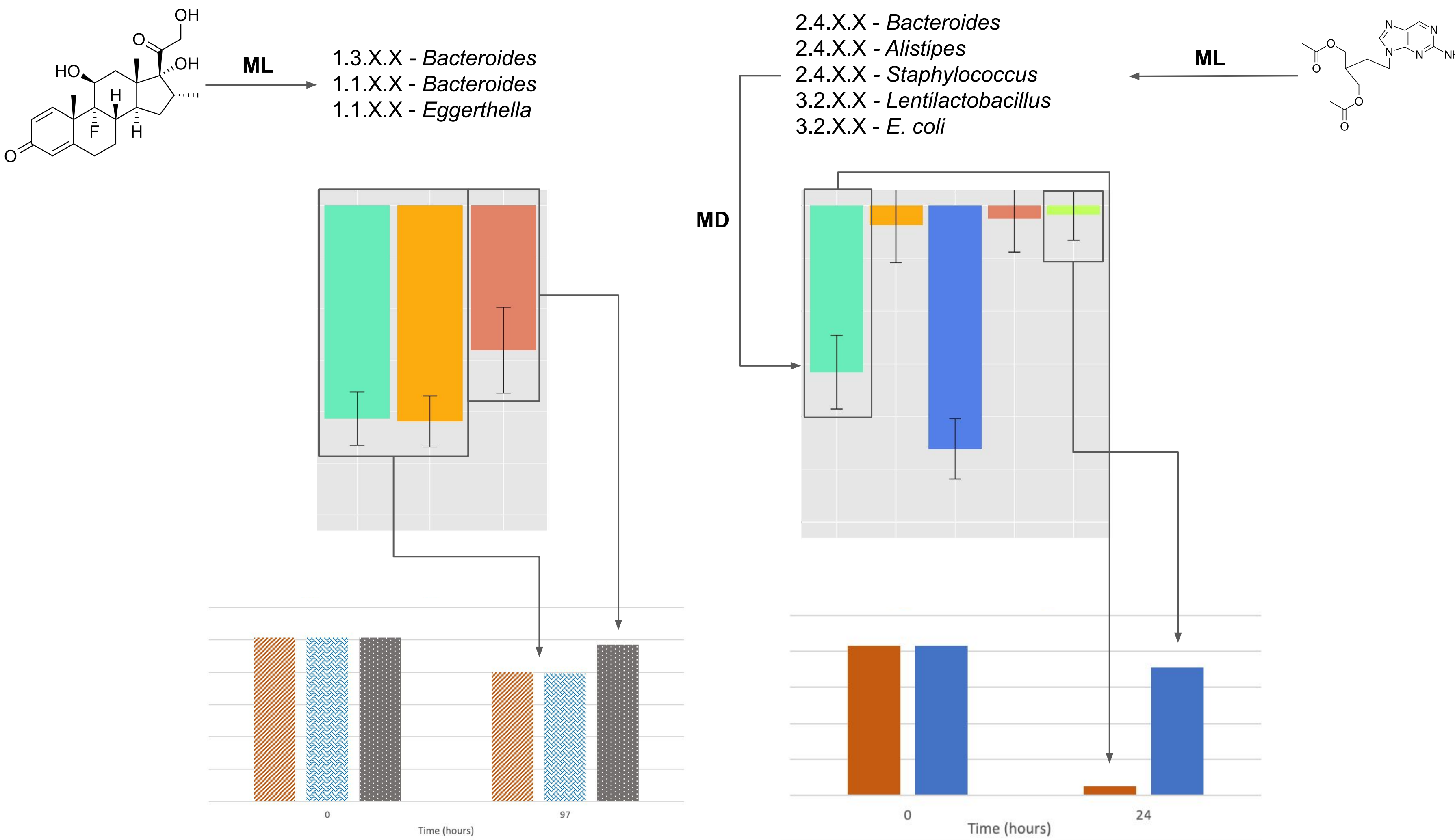
Filtering false positive predictions using molecular modeling



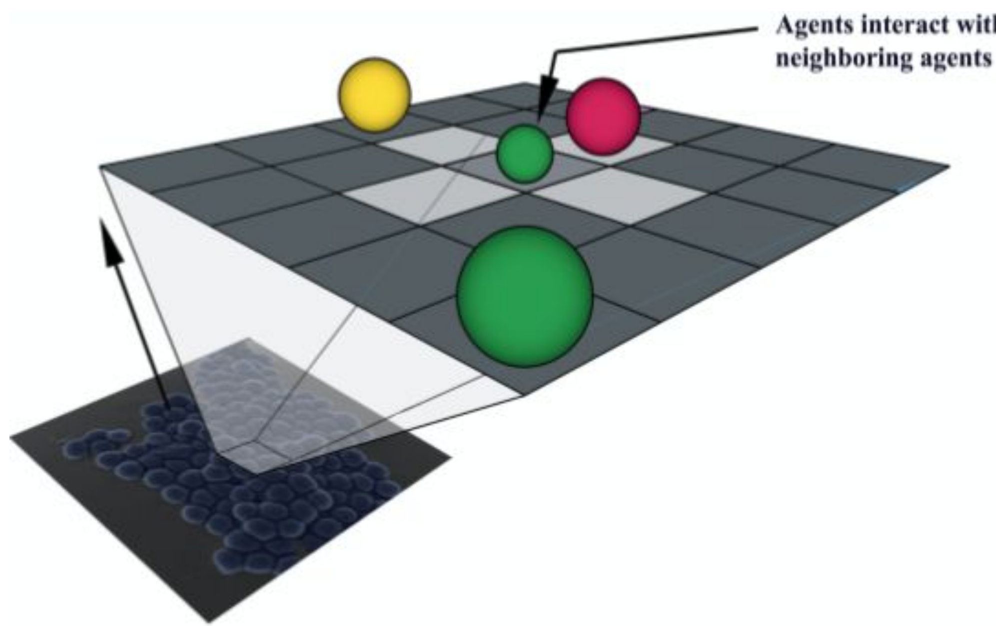
Full pipeline for prediction of metabolizing enzymes combining machine learning, structural similarity, and molecular modeling



Experimental validation of microbial metabolism predictions



Microbiome modeling for prediction of time-resolved degradation profiles



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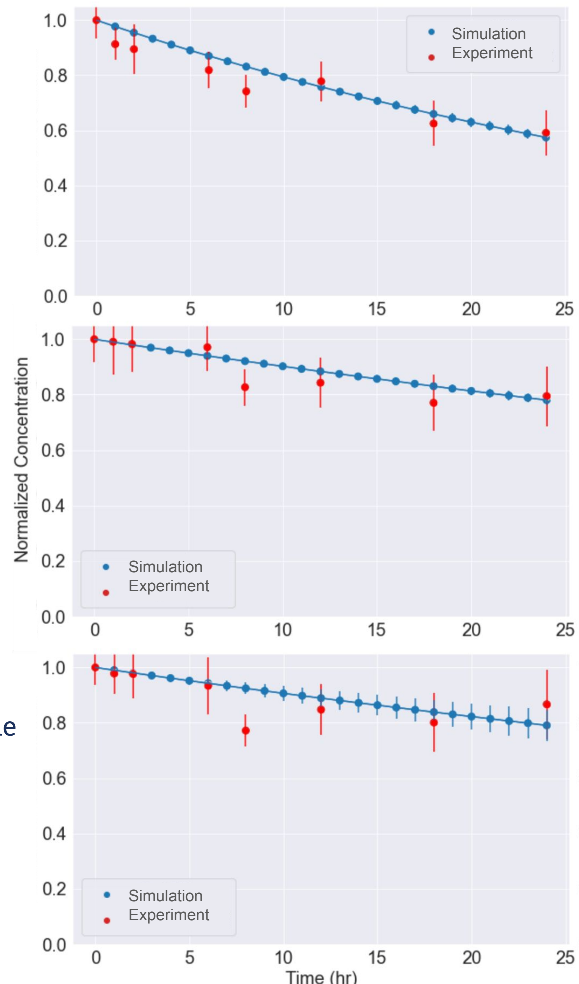
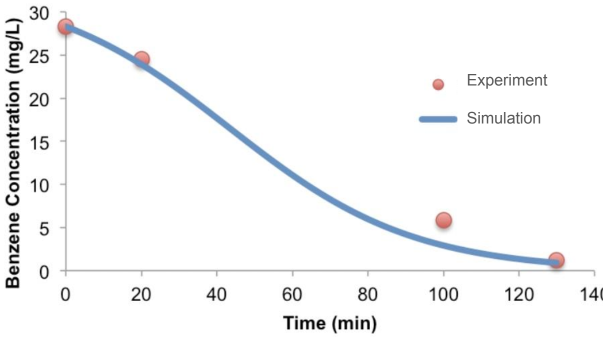
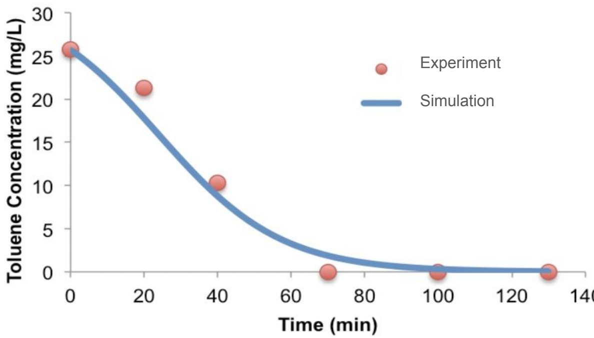
Precision Medicine







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